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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/620,691	07/20/2000	David A. Tirrell	30431.5US01	3160

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EXAMINER	
GUPTA, ANISH	
ART UNIT	PAPER NUMBER
1654	14

DATE MAILED: 03/06/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/620,691	TIRRELL ET AL.	
	Examiner	Art Unit	
	Anish Gupta	1654	

-- The MAILING DATE of this communication appears on the cover sh et with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) *5-14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restriction

1. Applicant's election of Group I in Paper No.13 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 5-14 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Group II, there being no allowable generic or linking claim. Election was made without traverse in Paper No. 13.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 3, it is unclear how the non natural amino acid is different in functionality from the functionality to the natural counterpart. Specifically it is unclear if the difference can be attributed to the side chain function in the protein, the charge of the side chain or structure.

In claim 1, it is unclear what constitutes as increased stability. Does increased stability make reference to a more stable three dimensional structure or enzymatic degradation.

In claim 4, hexafluorovaline is misspelled.

Claim 3 is improperly dependent on claim 1: Claim 3's preamble states that "The non-natural amino acid of claim 1". However, claim 1 is a polypeptide. Appropriate correction is requested.

In claim 1, it is unclear when and how many amino acids are to be substituted for a non-naturally occurring amino acids. That is if a protein or polypeptide contain five leucine resides, are all of leucine residues substituted, some of the residues are replaced or just one of the residues replace.

Written Description

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application relied on, of the specific subject matter later claimed by him. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP 2163.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In Regents of the University of California v. Eli Lilly & Co., the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials. Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606; In re Smythe, 480 F.2d 1376, 1383, 178 USPQ 279, 284-85 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus. . . ."). Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP further states that for if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP 2163. The MPEP does state that for generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP 2163. Although the MPEP does not define what constitute a sufficient number of representative, Court have indicated what do not constitute a representative number species to adequately describe a broad generic. In Gostelli, the Court determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. In re Gostelli, 872 F.2d at 1012, 10 USPQ2d at 1618.

In the instant case, the claims are drawn to a polypeptide wherein within the peptide leucine, isoleucine, or valine are substituted for a non-natural amino acid. The depended claims describe the non-natural amino acids a hydrophobic amino acid and further provide a markush group for the amino acid. The generic statement polypeptide or protein fails to adequately describe a structural feature common to the genus since the only common feature would be an amide bond between the amino acids. Further, the presence of isoleucine, leucine or valine would not be sufficient to form a common core since one could not readily envisage a representative number of examples with this common core. Further, the polypeptide and proteins of the claims are not limited to any specific class of compounds for which one could readily obtain physical and/or chemical properties or functional characteristics thereby obtaining some insight as to the structure

of the desired proteins or polypeptide. It is noted that the specification states that the proteins and polypeptide envisaged contain a hydrophobic core. However, the specification does not describe what amino acids and how many amino acids constitute this hydrophobic core. The specification, as a whole, does not sufficiently provide ample definition, such as by structure, formula, or chemical name, of the claimed subject matter sufficient to distinguish it from the desire proteins to other proteins. Accordingly, the disclosure lacks sufficient written description to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

As stated earlier, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable claim 1 is a broad generic with numerous variants. a protein or polypeptide encompass millions of compounds known art. The limitations of the presence of leucine, isoleucine, or valine does not substantially limit the number of species or variation of species encompassed by claims. Further, the claims are generic to peptides containing multiple amino acids to be replace but does not provide any guidance as which amino acids in isoleucine, leucine or valine should be substituted. That is, when a peptide containing several leucine residues, the specification does not provide any written description if all leucine residues, if some residues, or if one residue should be replaced. Further, if only some and one should be replaced, there is no disclosure as to which leucine residue is to be replace. This similar problem exists for a peptide that have several combinational residues of leucine, isoleucine, or valine. For this broad generic, the disclosure provide two specific examples in GCN4-p1 and A1 peptides. In these examples, a leucine residue is replaced with a trifluoroleucine or hexafluoroleucine residue in the GCN4 and A1 peptide. The specification does

not provide any species of polypeptide, beyond GCN4-p1 and A1 peptides nor does the specification provide any species of polypeptide where there are multiple or multiple combination of leucine, isoleucine, or valine. As stated above, if the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. The specification lack sufficient variety of species to reflect this variance. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, the examples provided in the specification cannot constitute written description to any protein and polypeptide as encompassed by the claims. Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> a person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Rennert et al.

The claims are drawn to a polypeptide wherein a leucine, isoleucine or valine are substituted with a non-natural amino acids.

The reference discloses the replacement of leucine with 5,5,5 trifluoroleucine in an E.coli B protein. (See page 471).

7. Claims 1 and 3-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Russel et al.

The claims are drawn to a polypeptide wherein a leucine, isoleucine or valine are substituted with a non-natural amino acids.

The reference discloses the replacement of valine with trifluorovaline or hexafluorovaline in an gramicidin a. (See page 202518, Abstract no. 104:202518).

8. Claims 1 and 3-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Arai et al.

The claims are drawn to a polypeptide wherein a leucine, isoleucine or valine are substituted with a non-natural amino acids.

The reference discloses the replacement of to valine residues in natural gramicind S with hexafluorovaline. (See abstract).

9. Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Mendel et al.

The claims are drawn to a polypeptide wherein a leucine, isoleucine or valine are substituted with a non-natural amino acids.

The reference discloses the replacement of a leucine with a S,S-2-amino-4-methylhexanoic acid in the 133 position in the T4 Lysozyme (See page 1799-1800). The S,S-2-amino-4-methyhexanoic acid is a hydrophobic amino acid.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anish Gupta whose telephone number is (703) 308-4001. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback , can normally be reached on (703)306-3220. The fax phone number of this group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Anish Gupta

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